REMARKS/ARGUMENTS

Claims 1-20 are pending.

Applicants note that page 25 of the Action is directed to a rejection under 35 USC 103, however the rejection does not list the claims that would be subject to such a rejection. As such, Applicants believe no response is necessary at this time.

Applicants also note that page 23 of the action refers to a rejoinder between product claims and process claims. As the present claims do not encompass products, Applicants believe this is not applicable to the instant application.

In response to the Restriction Requirement, Applicants elect the invention of Group II with traverse. Rejoinder of Groups I-IV is requested.

The Examiner has argued that the claims represent 10 separate inventions. Applicants respectfully submit that the present claims, particularly Claims 1-11, represent a single invention.

The Examiner has suggested that the features of dependent claims 4, 5 and 6 represent different inventions, when clearly they are embodiments of the same invention, i.e. species within the generic claim 1. Applicants respectfully submit that it is not proper to separate out the features of Claim 1 as if they were entirely different inventions. Claim 1 is a proper generic claim, and any restriction should at most require an election of species in the group, not a restriction to separate inventions.

While 35 U.S.C. 121 provides that restriction may be required to one of two or more independent and distinct inventions, 37 CFR 1.141 provides that a reasonable number of species may still be claimed in one application if the other conditions of the rule are met.

As discussed in MPEP 806.04(a), species, while usually independent, may be related under the particular disclosure. Where inventions as disclosed and claimed are both (A) species under a claimed genus and (B) related, then the question of restriction must be determined by both the practice applicable to election of species and the practice applicable to other types of restrictions such as those covered in MPEP § 806.05 - § 806.05(i).

It is not possible to define a generic claim with that precision existing in the case of a geometrical term (MPEP 806.04(d)). In general, a generic claim should include no material element additional to those recited in the species claims, and must comprehend within its confines the organization covered in each of the species. For the purpose of obtaining claims to

more than one species in the same case, the generic claim cannot include limitations not present in each of the added species claims. Otherwise stated, the claims to the species that can be included in a case in addition to a single species must contain all the limitations of the generic claim.

This is illustrated in the instant application by the fact that there is no categorization of claim 1 in its full breadth, i.e. the general method encompasses the use of all inhibitors of RAD52. As such, this should be recognized as an invention (method of promoting integration of a retroviral vector in a mammalian cell comprising inhibiting RAD52 DNA-binding activity in the cell), with sub-species that might be subject to a species election requirement, where the species claims have been properly presented as dependent on Claim 1, and therefore encompass its limitations.

Once a claim that is determined to be generic is allowed, all of the claims drawn to species in addition to the elected species which include all the limitations of the generic claim will ordinarily be obviously allowable in view of the allowance of the generic claim, since the additional species will depend thereon or otherwise include all of the limitations thereof.

A key determination in whether a generic claim is appropriate depends on the disclosure of a commonality of operation, function or effect. As stated in the present application there is a commonality of operation, function, and effect. A common operation in Claims 1-11 is a promotion of integration of a retroviral vector into the genome of a mammalian cell by inhibiting RAD52 DNA-binding activity. A common function in Claims 1-11 is the inhibition of RAD52 DNA binding activity. A common effect is the promotion of retroviral integration.

The Action has stated that *in vitro* and *ex vivo* methods require significantly different methods of practice. Applicants respectfully submit that such a distinction is entirely arbitrary. The distinction between a cell *in vitro* and a cell *ex vivo* also seems entirely arbitrary. How could a search of one not fully encompass a search required for the other? A cell *ex vivo* is a cell *in vitro*! There is no technical distinction relevant to the invention as to whether the cell is *ex vivo* or just *in vitro*.

The classification stated by the Examiner provides for no distinction between *in vitro* and *ex vivo* – in fact, subclass 93.2 (which is stated to apply to the "*in vitro*" aspects of the invention) reads:

> Genetically modified micro-organism, cell, or virus (e.g., transformed, fused, hybrid, etc.): Subject matter involving a micro-organism, cell or virus which (a) is a product of recombination, transformation, or transfection with a vector or a foreign or exogenous gene or (b) is a product of homologous recombination if it is directed rather than spontaneous or (c) is a product of fused or hybrid cell formation.

Nowhere in the subclass definition is there a differentiation between an *in vitro* and an *ex vivo* composition. As a cell *ex vivo* is *in vitro*, a search of one will necessarily have to encompass a search of the other. It cannot be expected that the Examiner would regard any art relating to cells "*ex vivo*" as not being relevant to cells "*in vitro*" or *vice versa*.

The Examiner suggests on page 4 that "The method of Invention I comprises using the method and cells *in vitro* wherein [*sic*] the method of Invention II is a method of gene therapy which requires significantly different methods of practice compared to using the method *in vitro*." (See also page 8 for II and III, and page 11 for III and IV.) However, for a cell *ex vivo* the steps encompassed by the present invention – inhibition of DNA-binding activity of RAD52 in a mammalian cell – are carried out *in vitro* (i.e. "in glass" – outside the body – *ex vivo*).

Insofar as the Examiner purports a method of "gene therapy" to be carried out on a body, it is requested that the actual language of the claims be reviewed. The claims are directed to the inhibition of DNA-binding activity of RAD52 in a mammalian cell outside the body to promote retroviral integration into the genome of the mammalian cell. Therefore, the claims do not recite a method of gene therapy.

Applicants submit that between the alleged groups I and II; or between the alleged groups III and IV; there is no technical distinction at all.

Furthermore, groups I and III and groups II and IV are incorrectly distinguished by the Examiner. The fact that any search of e.g. II should fully encompass IV is illustrated for a start by the fact that the Examiner has given identical classifications (pages 2-3 of the office action). Furthermore, the Examiner's reason on page 5 for alleging that inventions I and III are distinct is legally insufficient and erroneous. It is stated that "The method of Invention I inhibits production of RAD52 protein, the method of Invention III inhibits binding of DNA by RAD52 and requires materially different and separate protocols from the method of Invention I". However, both are embodiments of the generically claimed feature of "inhibiting RAD52 DNA-binding activity in the cell", a feature that the Applicants are properly entitled to have searched and examined – not least because it is believed to be patentable to do this to promote integration of a retroviral vector into the genome of a mammalian cell.

The data in the application provide support for the inventors' insight that only when Rad52 binds to retroviral DNA ends is there the observed effect on retroviral integration, so that anything that inhibits that binding will work to promote the integration. RAD52 DNA-binding activity can be inhibited by any means that physically inhibits RAD52 protein from binding DNA or which inhibits RAD52 protein from being present and available for binding DNA. It is

noteworthy that this is properly reflected in claim 1 and no "materially different and separate protocols" are claimed or need to be claimed.

It is noteworthy at this stage that the present invention is not concerned with a gene called "RAD52" in yeast, but a different gene in mammalian cells. Moreover, there is nothing in the prior art to make obvious the present invention as claimed relating to promoting retroviral vector integration into the genome of a mammalian cell in a method comprising inhibiting DNA-binding activity of RAD52 in the mammalian cell.

The Examiner is invited to consider carefully the discussion in the application of known phenotypic differences arising from mutation of the yeast gene known as RAD52 and the mammalian gene of the same name. See for example on page 2 where knockout experiments are described. Reading the introduction from the beginning through to page 7 provides a clear explanation of the novelty and unobviousness of the present invention, supported by the experimental data in the application.

Reconsideration is requested and rejoinder of at least groups I, II, III and IV.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number MEWE-016.

Respectfully submitted,
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